



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/607,809

06/27/2003

Leonard Katz

300622004810

6321

82359 7590 08/25/2009

Bristol-Myers Squibb Company

c/o MoFo

12531 High Bluff Drive, Ste. 100

San Diego, CA 92130

EXAMINER

ROBINSON, HOPE A

ART UNIT

PAPER NUMBER

1652

MAIL DATE

DELIVERY MODE

08/25/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/607,809	<b>Applicant(s)</b> KATZ ET AL.	
	<b>Examiner</b> HOPE A. ROBINSON	<b>Art Unit</b> 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 11 June 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 2,7-9 and 17-19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2, 7-9 and 17-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 October 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Application Status***

1. The Finality of the previous Office Action mailed on May 13, 2009 is withdrawn in favor of the following.
2. The amendment filed on August 11, 2009 has been received and entered.

### ***Claim Disposition***

3. Claims 2, 7-9 and 17-19 are pending and are under examination.

### ***Claim Objection***

4. Claims 18-19 are objected to because of the following informalities:  
Claim 18 is objected to because the claim does not further limit claim 2 from which it depends since both claims recite the organism "Streptomyces".

Claim 19 is objected to because the acronym "E. coli" does not appear with the corresponding spelled out meaning.

Correction is required.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
  2. Ascertaining the differences between the prior art and the claims at issue.
  3. Resolving the level of ordinary skill in the pertinent art.
  4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Art Unit: 1652

6. Claim 2, 7-9 and 17-19 rejected under 35 U.S.C. 103(a) as being unpatentable over Reeves et al. (U.S. Patent No. 6,759,536, October 2, 1998) in view of Gandecha et al. (Gene, vol. 184, pages 197-203, 1997).

Reeves et al. teach the use of vectors and host cells in a method that produces polyketide structures. Reeves et al. teach a loading module responsible for binding the first building block used to synthesize the polyketide and transferring it to the first extender module. Reeves et al. teach that the loading module of a DEBS consists of an acyltransferase (AT) domain and an acyl carrier protein (ACP) domain. Reeves et al. also teach another type of loading module that utilizes an inactivated ketosynthase (KS) domain an AT and ACP domains. This inactivated KS is called KS<sup>Q</sup>, where the superscript letter is the abbreviation for the amino acid, glutamine, that is present instead of the active site cysteine required for ketosynthase activity. In addition, Reeves et al. teach that other PKS enzyme, including the FK-506 PKS, the loading module incorporate an unusual starter unit and is composed of a CoA ligase like activity domain. Reeves et al. further teach that the loading module recognizes a particular acyl-CoA (usually acetyl or propionyl but sometimes butyryl or other acyl-CoA) and transfers it as a thiol ester to the ACP of the loading module (see paragraph 10). At paragraph (6) Reeves et al. teach fkbS (a crotonyl-CoA reductase involved in the biosynthesis of ethylmalonyl CoA) from the organism *Streptomyces*. Reeves et al. teach an acyl transferase domain specific for ethylmalonyl CoA. At paragraphs 54 and 56, Reeves et al. exemplifies multiple extenders. Paragraph 100 discloses a *Sacharopolyspora*. Paragraphs 153 and 155 disclose the use of *E. coli*. Reeves et al. teach a gene from

Art Unit: 1652

*Streptomyces hygroscopicus* however, does not teach the organisms *S. fradiae*, *S. cinnamomensis* or *S. collinus* recited in item (b) of claim 2. In-so-far-as Reeves et al. do not teach the aforementioned species, Gandecha et al. teach a *S. fradiae* containing orf4 (ccr) a crotonyl-CoA reductase, which converts acetoacetyl-CoA to butyryl-CoA for use as a 4C extender unit (see page 197).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have an isolated host cell comprising a recombinant polyketide synthase gene as characterized in the instant claim 2 because Reeves et al. teach the use of vectors and host cells in a method that produces polyketide structures using the fkbS gene of *Streptomyces hygroscopicus* (a crotonyl-CoA reductase (ccr) involved in the biosynthesis of ethylmalonyl CoA), see paragraph [0006]. Reeves et al. also disclose at paragraph [00161] that “for ethylmalonyl CoA biosynthesis, one requires only a crotonyl CoA reductase (ccr), which can be supplied by the host cell but can also be supplied by recombinant expression of the fkbS gene of the present invention. To increase yield of ethylmalonyl CoA, one can also express the fkbE and fkbU genes as well. While such production can be achieved using only the recombinant genes above, one can also achieve such production by placing into the recombinant host cell a large segment of the DNA provided by the cosmid of the invention. Thus, for 2-hydroxymalonyl and 2-methoxymalonyl CoA biosynthesis, one can simply provide the cells with the segment of DNA located on the left side of the FK-520 PKS genes shown in FIG. 1. For ethylmalonyl CoA biosynthesis, one can simply provide the cells with the segment of DNA located on the right side of the FK-520 PKS

Art Unit: 1652

genes shown in FIG. 1 or, alternatively, both the right and left segments of DNA”.

Reeves et al. does not teach the specific species claimed in the instant claims, however, Gandecha et al. discloses *S. fradiae*.

One of ordinary skill in the art would be motivated to substitute the *S. hygroscopicus* (ccr) as disclosed by Reeves with the *S. fradiae* (ccr) disclosed by Gandecha et. al. to arrive at the claimed invention as a whole since Reeves et al. teach that “for ethylmalonyl CoA biosynthesis, one requires only a crotonyl CoA reductase (ccr)” and Gandecha et al. identifies the same function the *S. fradiae* (ccr). Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

### ***Response to Arguments***

7. The response filed has been considered in full. Note that the rejection of record under 35 USC 102 is withdrawn based on applicant’s arguments. However, note that a new ground rejection has been instituted under 35 USC 103 for the reasons stated above.

### ***Conclusion***

Art Unit: 1652

8. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to HOPE A. ROBINSON whose telephone number is (571)272-0957. The examiner can normally be reached on Monday-Friday 9:00-6:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Hope A. Robinson/

Primary Examiner, Art Unit 1652